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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/604,876	06/28/2000	Mercy M. Davidson	0575/56614/JPW/JML/HA	6365

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/604,876	DAVIDSON, MERCY M.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cov r sh t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,8,9 and 12-19* is/are pending in the application.

4a) Of the above claim(s) *13-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,8,9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *28 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/3/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

An amendment was received and entered on 11/13/03.

Claims 1, 3-5, 8, 9, and 12-19 remain pending in the application. Claims 13-19 were withdrawn from consideration in Paper No. 7 as being drawn to a non-elected invention. Applicant timely traversed the restriction requirement which was subsequently made final.

Claims 1, 3-5, 8, 9 and 12 are under consideration in this Office Action.

Rejections Withdrawn

Applicant's amendments were sufficient to overcome the rejection of claims 1, 3-5, 8, 9, and 12,under 35 USC 112, first paragraph for lack of enablement. However, claims 8, 9, and 12 are newly rejected under 35 USC 112, first paragraph as discussed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 9, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of preparing a human undifferentiated immortalized cell line by fusing with human primary post-mitotic cells immortalized rho$^-$ fibroblasts that comprise a replicable nucleic acid vector that expresses SV40 large T antigen, and selecting for fused cells that have a functioning respiratory chain, contain the replicable nucleic acid vector expressing SV40 large T

antigen, are immortalized, and express one or more genes that are expressed specifically by the primary post-mitotic cells, does not reasonably provide enablement for methods of preparing a human undifferentiated immortalized cell line that does not express SV40 large T antigen, and does not express one or more genes that are expressed specifically by the primary post-mitotic cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claimed invention is a method of making an immortalized, undifferentiated cell line by fusing a human post-mitotic primary cell with a fibroblast immortalized with a replicable vector that expresses SV40 large T antigen. A review of the specification shows that the invention is intended to function as a method of immortalizing human primary post-mitotic cells that are difficult to immortalize, for the purpose of studying characteristics of the post-mitotic primary cells, or for use in therapeutic techniques. It follows that the cells produced by the method should have at least some functional or phenotypic characteristics of the parent human primary post-mitotic cells.

The focus of this rejection is step (e) which requires selecting a cell which contains "a nucleus which originated from the cell of the primary culture", but does not require that the selected cells must be immortal, nor does it require that the cells must resemble the parent human primary post-mitotic cells in any functional or phenotypic way. The Office interprets the claims as requiring that at least some part of the nucleus of the selected cell must have had its origin in the primary cell line. So, the limitation "a nucleus which originated from the cells of the primary culture" is considered to embrace

a scope ranging from nuclei that comprise the entire chromosomal complement of the primary culture, to nuclei that contain only a fragment of genetic material from the primary culture. Note that the claims do not recite any limitation regarding the determinants in the cytoplasm or nucleus that are responsible for the differentiation state of the cell. Because both fusion partners in the method are human cells, they must both contain at least some identical genetic material. For this reason, a fusion cell that retained only the nuclear chromosomal complement of the fibroblast, and none of the chromosomes of the primary cell, would still meet the limitations of the instant claims, because the fibroblast would reasonably be expected to contain at least some DNA that is identical to that of the primary cell, simply because they are both human cells. However, the specification does not teach how to use such a cell for the purposes set forth in the specification, i.e. research or therapeutic use of cells with characteristics of the primary post-mitotic cell, and one of skill in the art would have to perform undue experimentation in order to use such cells as intended. This portion of the rejection can be overcome by amending the claim to require selection of cells that express genes expressed specifically by the primary post-mitotic cell, as supported in the specification at page 8, lines 28-35.

In view of the specification at the paragraph bridging pages 22 and 23, fusion of the T-antigen vector-carrying fibroblasts with the primary cells is simply a means of delivering the T-antigen expression vector to the primary cells in order to immortalize them. It follows that the immortalized cells that are the product of the method should contain the T-antigen vector and express T-antigen. However, the instant claims do not

require that the produced cells must either contain the vector or express T-antigen. The scope of the method that embraces making cells that do not have the vector or express T-antigen is not enabled because the specification fails to teach how to immortalize cells without the use of a replicable vector that expresses SV40 large T antigen, and instead explicitly focuses on how to immortalize cells by delivering such a vector to cells. This rejection can be overcome by amending the claims to require that the selected cells must contain a replicable vector that expresses SV40 large T antigen.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3-5 stand rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (In Vitro Cellular and Developmental Biology 27(1): 63-74, 1/1991).

Wang teaches a human fetal cardiac myocyte cell line designated W1. This line is considered to be immortalized because it was maintained in culture for one year. See abstract. Claims 3-5 are included in the rejection because there is no apparent difference between these cells and the W1 line. For example, like the cells of claims 3-5, the W1 cells carry an expression construct encoding SV40 T antigen (pRSVTAg). See page 67, column 2, last complete sentence. The specification teaches that the cells of claims 3-5 express beta-myosin heavy chain, connexin-43, and desmin. Wang is silent as to whether or not the W1 cells express these markers. However, expression

of these proteins is considered to be an inherent characteristic of cardiomyocytes, and is therefore considered to occur in the W1 cells absent evidence to the contrary. The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989).

Response to Arguments

Applicant's arguments filed 11/13/03 have been fully considered but they are not persuasive.

Applicant argues that Wang fails to teach each and every feature of the claimed cell lines because Wang uses a process other than that which is claimed to produce the cells. This argument is unpersuasive because Applicant has presented no evidence to indicate that the cells of Wang are in any way different from those of the claimed invention. The cell line of Wang carries an expression construct encoding SV40 T antigen as do the instant cells, and expresses a cardiac myosin as do the claimed cells. See Table 2 of Wang and page 20, lines 9 and 10 of the specification. There is no evidence that the claimed cells differ from those of Wang by expressing any fibroblast marker (see page 20, lines 2 and 3). Because the PTO does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural

and functional characteristics of the claimed product, and because Applicant has failed to point to any specific difference between the cell lines, the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at 703-306-3217 before 2/22/04, and at 571-272-0811 after 2/22/04. The official central fax number is 703-872-9306 until further notice. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

DAVE T. NGUYEN
PRIMARY EXAMINER

Richard Schnizer, Ph.D.